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MICHELLE MAHER
NCI/DCPC
6006 Executive Blvd. Suite 321 MSC7058
ROCKVILLE, MD 20892-7058

ATTN:
PHONE: 301-496-0478
FAX: 301-435-8645
E-MAIL:

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PRELIMINARY REPORT

Menstrual Cycle Effect on Plasma Lipids

D. Yvonne Jones, Joseph T. Judd, Philip R. Taylor, William S. Campbell, and Padmanabhan P. Nair

In a study of 31 healthy women in which dietary intake and body weight were controlled, a significantly higher mean plasma cholesterol was observed in the follicular phase of the menstrual cycle compared to the luteal phase (mean difference of 8.4% during controlled dietary periods). Higher mean plasma triglycerides (mean difference of 7.4%) and lower HDL-cholesterol (mean difference of 5.8%) were also observed in the follicular phase of the controlled dietary study, although these differences were not consistently significant.

PREVIOUS STUDIES have shown fluctuations in plasma lipids associated with the menstrual cycle.[1-5] However, in none of these studies were diet and body weight controlled to eliminate the possibility of their influence on the plasma lipid changes observed.

MATERIALS AND METHODS

Patients

Healthy premenopausal women aged 20 to 40 years were recruited for this study. Of 37 women who passed a screening interview and physical examination and enrolled in the study, 31 women completed the entire study and their data are presented here. All reported regular menstrual cycles and no use of hormone preparations for at least one year prior to study. Subjects were randomized to dietary groups with ratios of polyunsaturated/saturated fatty acids (P/S) of 1.0 or 0.3, which were maintained throughout the study. After a baseline period of one menstrual cycle, each woman was placed on a high fat (40% energy from fat) diet for four menstrual cycles and then a low fat (20% energy from fat) diet for four cycles. During the controlled dietary periods, all meals were prepared in the study facility. Morning and evening meals were eaten on site in the presence of the study dietitians who served as a partial monitors of compliance. Midday and weekend meals were packaged for home consumption. Body weight was measured and recorded every weekday morning prior to breakfast as another method of assessing compliance and in order to adjust caloric intake to maintain a constant body weight over the study.

Methods

Morning fasting blood samples were collected during midfollicular and midluteal phases of the menstrual cycle (estimated from menses dates and daily basal body temperatures) during baseline and the last (fourth) menstrual cycle of the high and low fat diets. Plasma was stored frozen at −40°C for later analyses of plasma cholesterol and triglycerides by enzymatic colorimetric procedures[6,7] and HDL-cholesterol (HDL-C) after phosphotungstate-magnesium precipitation.[8] All samples from a subject were run in duplicate in the same analytic run along with a prepared chemical standard to calibrate the machine. The coefficient of variation between runs for cholesterol was 4%, and 12% for triglycerides. Absolute values for HDL-C are low using frozen plasma, although the comparisons between periods are valid. Total cholesterol and triglycerides were not affected by freezing. Analyses were conducted on one follicular and one luteal sample from each subject in each of the three dietary periods.

Statistics

Follicular-luteal differences within dietary periods were tested by paired *t*-tests and differences across dietary periods and between P/S groups by two-way repeated-measures ANOVA using the statistical software program (SAS).[9]

RESULTS

Both P/S groups are pooled in Table 1, since there were no significant differences in the menstrual cycle results between P/S groups. No significant effect of dietary treatment on the follicular-luteal differences was evident. General dietary fat influences on plasma lipids in these women have been reported elsewhere.[10] In all three dietary periods a significant drop in total cholesterol in the luteal phase was observed (mean decrease of 7.6% from follicular values). A drop in plasma triglycerides (3.6% in high fat period, 11.3% in low

From the National Cancer Institute, National Institutes of Health; and the Beltsville Human Nutrition Research Center, US Department of Agriculture.

Address reprint requests to D. Yvonne Jones, PhD, Blair Bldg, Room 601, National Cancer Institute, NIH, 9000 Rockville Pike, Bethesda, MD 20892-4200.

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Table 1. Follicular and Luteal Measures of Plasma Lipids in 31 Women During Baseline and 2 Controlled Dietary Regimens

	Menstrual Cycle Phase		
	Follicular	Luteal	Difference
Baseline			
Cholesterol	4.88 (0.14)	4.59 (0.17)	0.29 (0.11)*
HDL-C	1.68 (0.06)	1.68 (0.06)	−0.01 (0.04)
Triglycerides	0.65 (0.05)	0.65 (0.05)	−0.00 (0.04)
High fat			
Cholesterol	4.97 (0.18)	4.49 (0.19)	0.48 (0.14)**
HDL-C	1.51 (0.06)	1.61 (0.08)	−0.10 (0.04)**
Triglycerides	0.56 (0.03)	0.54 (0.03)	0.02 (0.03)
Low fat			
Cholesterol	4.43 (0.16)	4.11 (0.17)	0.32 (0.12)**
HDL-C	1.37 (0.06)	1.44 (0.06)	−0.07 (0.04)
Triglycerides	0.71 (0.05)	0.62 (0.05)	0.08 (0.04)*

Values are given as means (mmol/L) with SE values in parentheses.
*$P \leq 0.05$.
†$P \leq 0.01$.

fat period) and a rise in HDL-C (6.6% in high fat, 5.1% in low fat) was seen in the controlled dietary periods but not at baseline.

DISCUSSION

The design of this study allows one to observe plasma lipid values at the midfollicular and midluteal phases of the menstrual cycle while maintaining constant dietary intake and body weight. Under these conditions, a significant decrease in controlled mean plasma cholesterol was observed in the luteal phase. The magnitude of this difference (0.29 to 0.48 mmol/L) is similar to previous reports.[1,4,5] as is the degree of HDL-C increase (0.01 to 0.10 mmol/L).[5] The changes in plasma lipids observed here may be attributed to the known effects of estrogen administration on lipoproteins. Estrogen has been shown to increase the concentration of the alpha-lipoproteins and decrease beta-lipoproteins,[11] presumably by increased uptake of LDL by the liver.[12] The triglyceride results would follow from decreases in the VLDL and LDL fractions, these being the primary carriers of triglycerides. During the menstrual cycle, estrogen levels peak just prior to ovulation and average higher levels during the luteal phase of the cycle compared to the follicular. These estrogen changes are consistent with the timing of the plasma lipid responses, particularly when the half-lives of about four days for LDL[13] and HDL[14] are considered. These results indicate that there is a hormonal effect on cholesterol levels and that this effect is independent of P/S ratio and relative fat intake when weight is held constant. A similar effect on serum triglyceride levels is suggested but appears to be influenced somewhat by dietary fat.

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